

Risk of taking oral contraceptives in patients with a history of migraine with neurological signs



Clinical question

“What is the risk of taking oral contraceptives in patients with a history of migraine with transient neurological signs?” A woman with a history of migraine associated with hemiparaesthesia, and possibly dysphasia, attended her general practitioner suffering from irregular and frequent menstrual cycles. The doctor considered treatment with oral contraceptives to control her cycles and possibly relieve her migraine attacks. He asked about the risk of treatment with oral contraceptives, compared with no treatment, in a patient with transient neurological signs associated with migraine.



Search question

The interventions of interest were oral contraceptives. Ideally, we sought evidence from prospective follow-up studies of women taking oral contraceptives (OCs), in which groups were compared according to relevant outcomes. Case-control studies are a good research design to investigate the association between common exposures and rare outcomes, as in the current question. Unfortunately, this design is also subject to a range of possible biases that can distort the findings — recall bias, observation bias and various biases involving subject and control selection.



Search

PubMed and the *Cochrane Library* were searched for relevant articles with English abstracts published since 1989. Search terms included “migraine” combined with terms for oral contraceptives (“contraceptive agents”; “contraceptive agents, female”; “contraceptives, oral”; “contraceptives, oral, combined”; “contraceptives, oral, hormonal”; “contraceptives, oral, synthetic”, “contraceptives, oral, sequential”; “progestational hormones, synthetic”), and “stroke” or “cerebrovascular disorders.”



Summary of findings

This evidence search demonstrated the difficulties involved in, firstly, assessing the incidence of adverse effects of treatments and, secondly, in conveying these data to patients. We found no prospective studies comparing stroke risk in women taking OCs who did and did not have a history of migraine. Similarly, we found no prospective studies comparing stroke risk in women taking OCs who experienced migraine with neurological signs and those taking OCs who experienced uncomplicated migraine.

Nevertheless, other kinds of evidence suggested that women taking OCs who had a history of migraine have a markedly increased relative risk of ischaemic stroke,

although the difference in absolute numbers of women affected may not be as marked.

- ▶ A case-control study of women aged 20–44 years¹ found that the relative risk of ischaemic stroke in women with migraine and taking OCs was 16.9 times (95% CI, 2.72–106) that of women without migraine and not taking OCs. Women with migraine who used low dose OCs (< 50 µg oestrogen) had 6.59 times (95% CI, 0.79–54.8) the risk of ischaemic stroke than women without migraine who did not take OCs, but this estimate came from a small number of cases and did not reach statistical significance. The relative risk of ischaemic stroke in women with migraine who took OCs and smoked cigarettes was 34.4 times higher (95% CI, 3.27–361) than in women with none of these risk factors.
- ▶ Similar results were found in a case-control study of women younger than 45 years.² Ischaemic stroke was 13.9 times more likely (95% CI, 5.5–35.1) in women with migraine and taking OCs than in women without migraine and not taking OCs.
- ▶ A pooled analysis of two US population-based case-control studies³ found that women currently taking OCs who had a history of migraine were only twice as likely (95% CI, 1.19–3.65) to have any kind of stroke than women not taking OCs who did not have migraines. While this supports the general finding, it quantifies a much lower increased risk.

The evidence from the identified research for an increased risk of stroke in these circumstances is convincing, but the size of the effect remains in dispute. Interpretation of the evidence in this case was complicated because the studies did not allow calculation of absolute-risk differences between groups. In giving advice to patients, the known increased relative risks for individuals must be balanced against the absolute effects at a population level. The identified studies show not only an increased relative risk of ischaemic stroke in women with migraine who take OCs, but also a greater than multiplicative increased risk introduced by coexistent smoking. On the other hand, since the overall risk of stroke for women in this age group is small (5.5 per 100 000 woman-years according to the World Health Organization Collaborative Study⁴), and is smaller still in younger age ranges, the observed risk estimates suggest ischaemic stroke will be a comparatively rare outcome in any of the identified risk groups. Clinical advice should incorporate these data as well. The ultimate decision remains with the patient.



Outcome

The patient was treated with OCs pending the outcome of the evidence search and gained relief of her gynaecological

symptoms. However, she decided to discontinue taking OCs when the evidence became available.

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Department of Health and Aged Care. Information about the project, including clinical questions and answers, can be found at <<http://www.med.monash.edu.au/healthservices/cce/>>

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Acknowledgements

This search was conducted as part of a project supported by a General Practice Evaluation Project grant, GPEP 720, the AQUA project, from the Commonwealth

(Received 2 Apr, accepted 23 Jul 2001)

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